A Preliminary Report on the Pattern of Plasma Homocysteine-Protein Ratio among Pregnant Women in Lagos, Nigeria

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Summary

In plasma, homocysteine (Hcy) is majorly bound to protein, and have been significantly associated with adverse obstetric outcomes such as placental abruption or placental infarction, unexplained recurrent fetal loss, and pre-eclampsia among others; including the possibility of predicting women at risk of these conditions.Estimated Hcy levels have been observed to vary significantly with age, sex, lifestyles, hereditary factors, and ethnicity among several other confounding factors. However, the evaluation of homocysteine-protein ratio (Hcy/Pro) may provide a more reliable biomarker by adjusting for variations in serum proteins. The aim of the study was to determine the pattern of Hcy/Pro among pregnant Nigerian females and evaluate possible associations with some haematological variables (Haemoglobin-Hb; Mean cell volume-MCV; Mean cell haemoglobin concentration-MCHC; White blood cell count-WBC and Platelet count-PLT).This study was an observational, hospital based, Cross-Sectional study comprising 130 pregnant women (cases) and 130 non-pregnant women (controls). The participants were recruited from the Lagos University Teaching Hospital (LUTH).Structured questionnaires were applied to obtain demographic, medical, socio-economic, and nutritional histories. Plasma Hcy was evaluated using Enzyme linked Immunosorbent Assay (ELISA), and Plasma protein was evaluated using a fully automated Beckman Synchron LX20 by Beckman Coulter, Inc., 250 S. Kraemer Blvd. Brea, CA 92821, USA. Statistical analyzes were performed using SPSS version 23. Reference range for Hcy/Pro for non-pregnant females was estimated to be 0.050 – 0.098µmol/g. Homocysteine-protein ratio was observed to decline progressively throughout pregnancy (F=36.565; p=0.0001). The mean Hcy/Pro of control group participants (0.074 ± 0.012 µmol/g) was significantly higher than the 0.057 ± 0.019 µmol/g reported for the study group (p=0.001). Homocysteine-protein ratio correlated negatively with gestational age (GA) of study group participants (r= - 0.364; p=0.003).The Hcy/Pro showed a progressive decline throughout pregnancy, compared to total plasma Hcy pattern, and may be a truer reflection of plasma homocysteine pattern in pregnancy.

Keywords:Homocysteine-protein ratio, homocysteine, pregnancy, proteins

Introduction

Homocysteine levels have been documented to fall in early pregnancy and are significantly reduced compared to the non-pregnant state as reported in most studies (1,2). The physiology behind this observation appears to be multi factorial as suggested by earlier researchers, and have been related to hormonal changes, haemodilution, physiological changes in serum albumin, increased renal clearance of homocysteine, increased folic acid supplementation and enhanced fetal utilization of methionine during pregnancy (3-5).

Very few studies have documented reference ranges for homocysteine in healthy adult females. Homocysteine in the range of 5-15 µmol/L was considered to be within physiological range for healthy adult females in a Korean population study (6). It has been documented that lowering the Hcy level by approximately 25% could result in significant reduction in cardiovascular risk (6,7). However, accurate evaluation of Hcy levels has its challenges, as it has been observed to vary significantly with age, sex, lifestyles, hereditary factors, and ethnicity among several other factors (6,8). In women, elevated levels of total homocysteine have been observed, and significantly associated with pathological pregnancy states such as placental abruption or placental infarction, unexplained recurrent fetal loss, and pre-eclampsia among others (9,10). However, some studies have not been able to replicate similar findings in some of these obstetric disorders (11,12). These inconsistencies could have resulted from multiple confounders during Hcy estimations. There is therefore a need to identify techniques and methods to eliminate identifiable confounders in the estimation of Hcy.

Albumin is considered the dominant binding protein for Hcy. In human cells, homocysteine exists primarily in its reduced form. However, in plasma, only about 1% of homocysteine exist in the reduced form. The Reduced free (unbound) homocysteine with its free thiol group, is the most reactive form of Hcy. The reduced Hcy participates in a wide range of redox reactions, including auto-oxidation at physiological pH, to form a disulfide bond between two homocysteine molecules or with proteins (13). About 70-80% of plasma homocysteine is bound to albumin (14,15). Therefore, at any given time in the plasma, Hcy exists as reduced homocysteine, oxidized homocysteine (homocystine, homocysteine disulfide-cysteine) and a protein-bound Hcy fraction. The physiologically active reduced Hcy is said to be highly unstable, and difficult to estimate due to significant variability and low concentrations

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